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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WHITEMAN, BRIAN A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 09/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/729,264	WELCHER ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10,48,57-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10,48,57 and 58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Non-Final Rejection

Claims 1-8, 10, 48, and 57-58 are pending.

Applicant's traversal, the amendment to claims 1, 2, 3, and 10, and the cancellation of claims 11 and 59 in paper filed on 7/16/04 is acknowledged and considered.

Claims 8 and 10 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim: 1) cannot depend on multiple claims with different features, 2) should refer to other claims in the alternative only, and 3) cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Claims 8 and 10 refer to two sets of claims to different features; does not refer to other claims in the alternative only and depends from other multiple dependent claims.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-8, 10, 48, and 57-58 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by a substantial or well-established utility.

The specification discloses a polynucleotide sequence, which encodes a B7-like polypeptide as set forth in SEQ ID NO: 2, 4, or 6. The specification further discloses an isolated nucleic acid sequence encoding a protein having B7-like activity (SEQ ID NO: 1, 3, or 5). The

specification fails to disclose any particular function or biological significance for the claimed B7-like nucleotide sequences.

The specification contemplates using B7-like polynucleotides for producing knock-out or knock-in non-human animals for drug candidate screening (page 75). The specification further contemplates that exposure of said animals to a drug may decrease or increase expression of the protein encoded by a B7-like gene and may be associated with a disease or a pathological condition. The specification further contemplates using DNA microarrays to identify and validate B7-like genes in disease and as targets for therapeutics molecular toxicology of B7-like molecules and inhibitors thereof; stratification of populations and generation of surrogate markers for clinical trials, and enhancing B7-like small molecules drug discovery by aiding in the identification of selective compounds in high throughput screens (page 76). The specification contemplates using B7-like genes or products directly or indirectly made from the gene to treat diagnosis, ameliorate or prevent acute or chronic disease associated with T-cell function (pages 95-98).

The claims are drawn to a polynucleotide sequence encoding a B7-like protein, which has no determined function or biological activity. At the time the invention was made, it was known that the function a B7 polypeptide was very diverse, and the B7 family of co-stimulatory molecules comprises B7.1 and B7.2 proteins, both of which can interact with two receptors, CD28 and CTLA-4, that are expressed by T cell proliferation, increasing evidence indicates that they may not deliver identical signals to T cells, and that they may skew Th1 and Th2 phenotypes (Li et al. Human Immunology, Vol. 61: 486-498, 2000). The as-filed specification provides no nexus between the 'association' of the claimed B7-like polynucleotide sequences

with the B7 family of co-stimulatory molecules. The specification does not define B7-like activity, a B7-like polypeptide or a B7-like gene.

With respect to using the claimed sequences or products made directly or indirectly from the sequences in either an *in vitro* or an *in vivo* screening assay comprising observing an increase or a decrease of the claimed B7-like gene products or another gene product, the specification does not teach what to look for as a result of an increase or a decrease B7-like expression. One skilled in the art would have to further experiment on the invention to determine what results are observed with either an increase or a decrease in B7-like expression. In absence of the specification teaching what to look for in the assays, the claimed invention lacks utility.

In addition, with respect to using the claimed B7-like polynucleotide sequences or products made directly or indirectly from the sequences to treat diagnosis, ameliorate or prevent acute or chronic disease associated with T-cell function, the specification provides no evidence that the B7-like proteins are involved to T-cell function. The specification provides no evidence that the claimed polynucleotide sequences are associated with any specific disease. It would require further experimentation on the claimed invention/or products made directly or indirectly from the sequences to determine whether they were involved in T-cell function or any disease. Thus, the asserted utilities set forth above do not provide a benefit to the public in currently available form. See Ziegler, 992 F.2d at 1203, 26 USPQ2d 1600 (Fed. Cir. 1993).

At page 73, lines 7-9 of the specification, the protein encoded by SEQ ID NO: 14 (an ortholog of SEQ ID NO: 1, 3 and 5) showed seminal vesicle hyperplasia in a transgenic mouse, however, this is not a disclosure of how to use the polypeptide sequence set forth in SEQ ID NO: 2, 4 or 6 (or the DNA molecule set forth in SEQ ID NO: 1, 3 or 5). SEQ ID NO: 14 has 23-24%

sequence identity with SEQ ID NO: 1, 3 or 5. The specification and the art of record are absent that seminal vesicle hyperplasia in a transgenic mouse whose genome comprises SEQ ID NO: 14 is considered a B7 activity. The office conducted a sequence search of the polypeptide sequences set forth in SEQ ID NO: 2, 4, and 6 against amino acid public databases and the results from the search did not display any sequence similarity with a known B7 protein. In addition, sequences with the closest sequence similarity with SED ID NO: 2, 4 or 6 were proteins with completely different functions than a known B7 function. For example, Neeper et al., teach a polypeptide that functions as a cell surface receptor for advanced glycosylation end product (AGE) (JBC, Vol. 267, pp. 14998-15004, 1992). The polypeptide sequence taught by Neeper has 22.6% sequence similarity with amino acids 15-349 of SEQ ID NO: 2; 23.5% sequence similarity with amino acids 64-353 of SEQ ID NO: 4; 23.3% sequence similarity with amino acids 9-353 of SEQ ID NO: 6.

Since the claimed invention is not supported by either a substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention. See also In re Kirk, 376 F.2d 936, 153 USPQ 48 (CCPA 1967) and In Brenner v. Manson, 383 US 519, 148 USPQ 689 (1966). Also see REVISED INTERIM UTILITY GUIDELINES TRAINING MATERIALS: www.uspto.gov/web/menu/utility.pdf.

Applicant's arguments filed 7/16/04 have been fully considered but they are not persuasive.

Applicant argues that the office has recognized the applicants have asserted that the claimed nucleic acid molecules may be used to encode polypeptides having B7-like activity.

Applicant's argument is not found persuasive because the office did not recognize that the claimed nucleic acid molecule encodes polypeptides having B7-like activity, the office only recited what the specification asserted. The rejection recites that neither the specification nor the prior art define B7-like activity, a B7-like polypeptide or a B7-like gene. In addition, applicants have removed the term "B7-like" from the claims in view of 112 second paragraph rejections on the term in prior office actions. Therefore, without knowing any B7-like activity observed by expressing the claimed nucleic acid molecules, one skilled in the art would not know how to use the claimed invention.

Applicant further argues that the claimed subject matter encompasses nucleic acid molecules encoding B7-like polypeptides, while the broad class of the invention is nucleic acid molecules. The present application asserts a utility that not all polynucleotides sequences would encode B7-like polypeptides.

Applicant's argument is not found persuasive because while it is acknowledged that not all polynucleotides would encode B7-like polypeptides, neither the specification nor the prior art define the term "B7-like polypeptide". The specification and the prior art do not teach any known activity of the B7-like polypeptides encoded by the claimed isolated nucleic acid molecules that could be associated with any method contemplated in the specification.

Applicant argues that B7-like proteins has a "real world' use regulating innate immune responses and thus treating various diseases states and conditions.

Applicant's argument is not found persuasive because the rejection of record has already addressed this argument. The argument merely recites what the specification recites and does not provide any additional evidence or guidance for how B7-like proteins can be used to regulate

any innate immune response or what specific diseases and conditions can be treated using B7-like proteins. The argument does not address that the as-filed specification provides no nexus between the 'association' of the claimed B7-like polynucleotide sequences with the B7 family of co-stimulatory molecules.

As stated in the rejection, the specification provides no evidence that the claimed polynucleotide sequences are associated with any specific disease. It would require further experimentation on the claimed invention/or products made directly or indirectly from the sequences to determine whether they were involved in T-cell function or any disease. Thus, the asserted utilities set forth above do not provide a benefit to the public in currently available form. See Ziegler, 992 F.2d at 1203, 26 USPQ2d 1600 (Fed. Cir. 1993).

Applicant argues that asserted utility is credible because the human B7-like proteins are homologous to the murine B7-like proteins and further teaches that the homologous B7-like murine protein induces seminal hyperplasia in transgenic mice.

Applicant's argument is not found persuasive because the rejection already addressed this issue and the applicant has not provided any additional evidence or support to overcome the rejection of record.

The specification and the art of record are absent that seminal vesicle hyperplasia in a transgenic mouse whose genome comprises SEQ ID NO: 14 is considered a B7 activity.

Furthermore, the office conducted a sequence search of the polypeptide sequences set forth in SEQ ID NO: 2, 4, and 6 against amino acid public databases and the results from the search did not display any sequence similarity with a known B7 protein. In addition, sequences

with the closest sequence similarity with SED ID NO: 2, 4 or 6 were proteins with completely different functions than a known B7 function.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8, 10, 48, 57, and 58 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a well asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Applicant's arguments filed 7/16/04 have been fully considered but they are not persuasive for the reasons set forth in the response to applicant's argument against the 101 rejection.

Claims 1-8, 10, 48, and 57-58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The limitation ' a nucleotide sequence that hybridizes to the complement of the nucleotide sequence of either (a) or (b) at 65°C in a hybridization buffer comprising 0.015M

sodium chloride and 0.0015M sodium citrate' in step (c) of amended claims 1-3 is not supported by the as-filed specification. There appears to be no written description in the application as filed for the limitation 'a nucleotide sequence that hybridizes to the complement of the nucleotide sequence of either (a) or (b) at 65°C in a hybridization buffer comprising 0.015M sodium chloride and 0.0015M sodium citrate'. See MPEP § 2163.06. Page 27, lines 20-23 in the instant specification is cited by applicant for support of the amended claims, but this page does not disclose the limitation in claims 1-3 as amended. On page 27, lines 20-23, applicants teach: "Examples of "highly stringent conditions" for hybridization and washing are 0.015M sodium chloride, 0.0015M sodium citrate at 65-68°c or 0.015M sodium chloride, 0.0015M sodium citrate, and 50% formamide at 42°C". Page 27 provides support for the limitation '"highly stringent conditions" for hybridization and washing are 0.015M sodium chloride, 0.0015M sodium citrate at 65-68°c or 0.015M sodium chloride, 0.0015M sodium citrate', but this page does not provide support for the limitation in step (c) in the amended claims. It is apparent that the applicants at the time the invention was made did not intend or contemplate the nucleotide sequence cited in step (c) of the claims and claims dependent therefrom as part of the disclosure of their invention. There is no evidence in the specification that the applicants were in possession of the claimed nucleotide sequence as set forth in the claims, as it is now claimed, and claims dependent therefrom at the time the application was filed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Hillier et al. (GenBank Accession No. N47851, US National Library of Medicine, Bethesda, MD, February 1996, accessed by PTO on 9/21/04).

Hillier anticipates claims 1-3 because Hiller teaches a nucleotide sequence that hybridizes to the complement of the nucleotide sequence of any SEQ ID NO: 1, 3 or 5 at 65°C in a hybridization buffer comprising 0.015M sodium chloride and 0.015M sodium citrate. See nucleotides 73-172 of N47851.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, SPE - Art Unit 1635, can be reached at (571) 272-0760.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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